Final Analysis of the Phase 1a/b Study of Fibril-Reactive Monoclonal Antibody 11-1F4 (CAEL-101) in Patients with AL Amyloidosis

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CAEL101 Directly Targets AL Amyloid

- Amyloid-fibril reactive monoclonal antibody IgG1κ 11-1F4
  - recognizes a conformational neoepitope
  - dissolution of human λ and κ amyloidomas in mice

- Chimerized GMP-grade amyloid fibril-reactive IgG1 11-1F4 mAb (CAEL-101) was produced by NCI's Biological Resource Branch

- Open-label, dose-escalation phase 1a/b study for patients with relapsed or refractory AL Amyloidosis

Study Objectives

Primary Objective:

- Establish the maximum tolerated dose (up to 500 mg/m^2)

Secondary Objectives:

- Demonstrate reduction in amyloid burden
- Determine the pharmacokinetics and safety at different dose levels
- Determine whether there is a dose response at the highest doses

Eligibility

KEY INCLUSION CRITERIA

- **Confirmed diagnosis of AL amyloidosis**
- **Received prior systemic therapy**
- **Does not require plasma cell targeted therapy**
- **Age** > 21 years
- **ECOG performance status** ≤ 3

KEY EXCLUSION CRITERIA

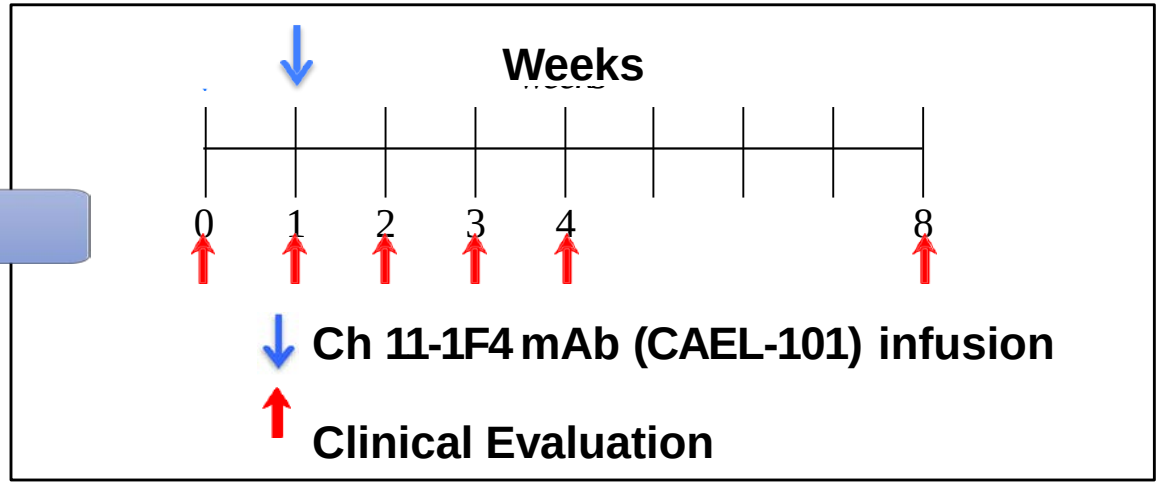
- **EF** < 40%
- **Intraventricular Septum** > 25mm
- **Creatinine clearance** < 30 cc/min
- **Alkaline phosphatase** > 3 times institutional upper limit of normal
- **Bilirubin** > 3.0 mg/dL

Dose Escalation

Level	Dose (mg/m²)
-2	0.125
-1	0.25
1	0.5*
2	5
3	10
4	50
5	100
6	250
7	500

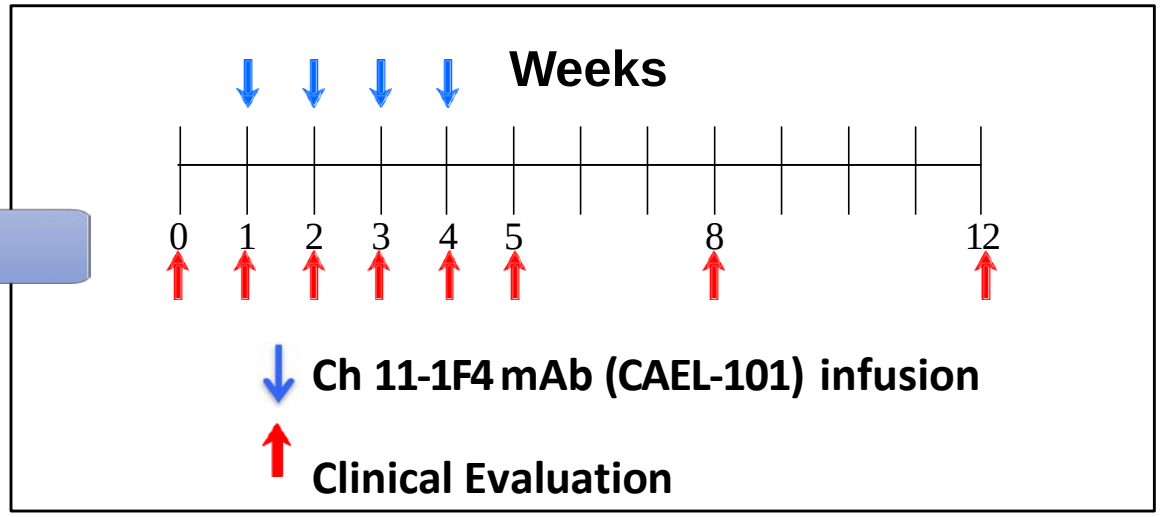
Phase 1a

- 8 patients



Phase 1b

- 19 patients



Patient Characteristics

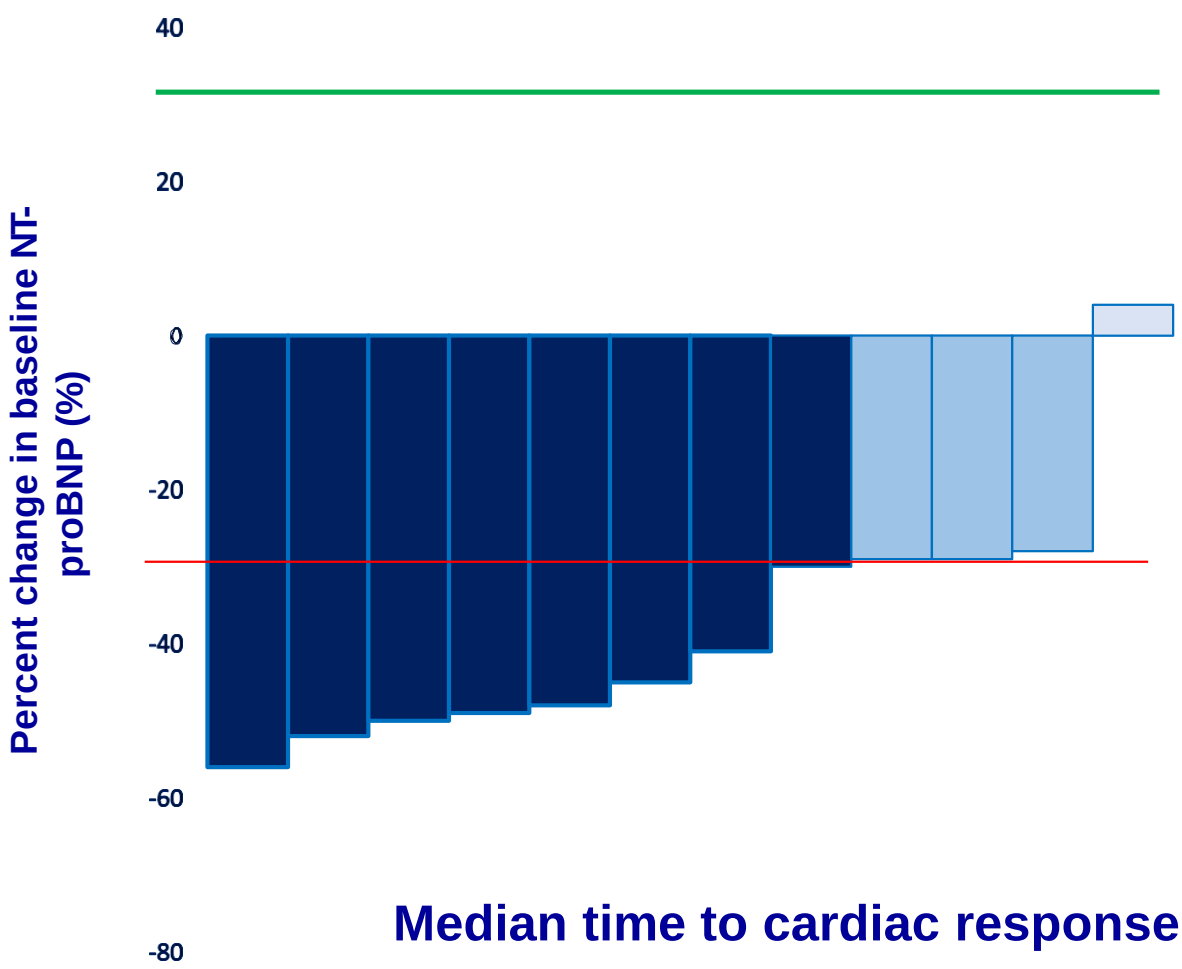
Characteristic	Median	
Age (N=27 patients)	66 yrs (Range: 34 – 79)	
Gender		Male N=19 (70%) Female N=8 (30%)
Light Chain type		λ N=15 (56%) κ N=12 (44%)
Revised Mayo Stage	II (Range: I to IV)	
Organ Involvement (No.)	2 (Range: 1 – 4)	Heart N=16 (59%) Kidney N=13 (48%) Skin/Soft tissue N=12 (44%) GI N=8 (30%) Nervous system N=3 (11%) Liver N=3 (11%) Musculoskeletal N=3 (11%) Lung N=1 (4%)
Best Hematologic Response to Plasma Cell Directed Therapy		CR N=4 (15%) VGPR N=19 (70%) PR N=2 (7%) NR N=2 (7%)
Previous Plasma cell Directed Therapy (No.)	2 (Range: 1 – 9)	1 Regimen 30% (N=8), 2 Regimen 30% (N=8), ≥3 Regimen 40% (N=11)
Baseline NT-proBNP (ng/L)[a]	1915 (Range: 815.5 – 8274)	
Baseline 24 hr Urine Protein (mg/24hr)[b]	4796 (Range: 1078 – 10,260)	
Time Since last Exposure to Chemotherapy (mos)	6 (Range 1 – 51)	

[a] Baseline NT-proBNP in patients with cardiac involvement who were evaluable for response (Baseline NT-proBNP≥ 650pg/mL)
[b] Baseline 24 hour urine protein in patients evaluable for renal response

Phase 1a/b Results

- **27 patients accrued and evaluable for toxicity**
  - No dose limiting toxicity to a Maximum tolerated dose of 500mg/m^2
  - No drug-related deaths
- **24 Patients evaluable for response**
  - N = 3 had no measurable disease
- **67% (12 out of 18 patients) with cardiac and/or renal involvement showed a response**
- **3 Patients with involvement of other organs had response**
  - 1 GI response (n = 4)
  - 1 Liver response (n = 2)
  - 1 soft tissue response with improvement of arthritis Grade 3→→1 (*n = 4*)
- **Overall Median Time to response** was **3 weeks** after the first dose of CAEL-101

Best Cardiac Response After Treatment with CAEL-101



PROGRESSION

>30% and >300 pg/ml increase in NT-proBNP

STABLE

RESPONSE

>30% and >300 pg/ml decrease in NT-proBNP

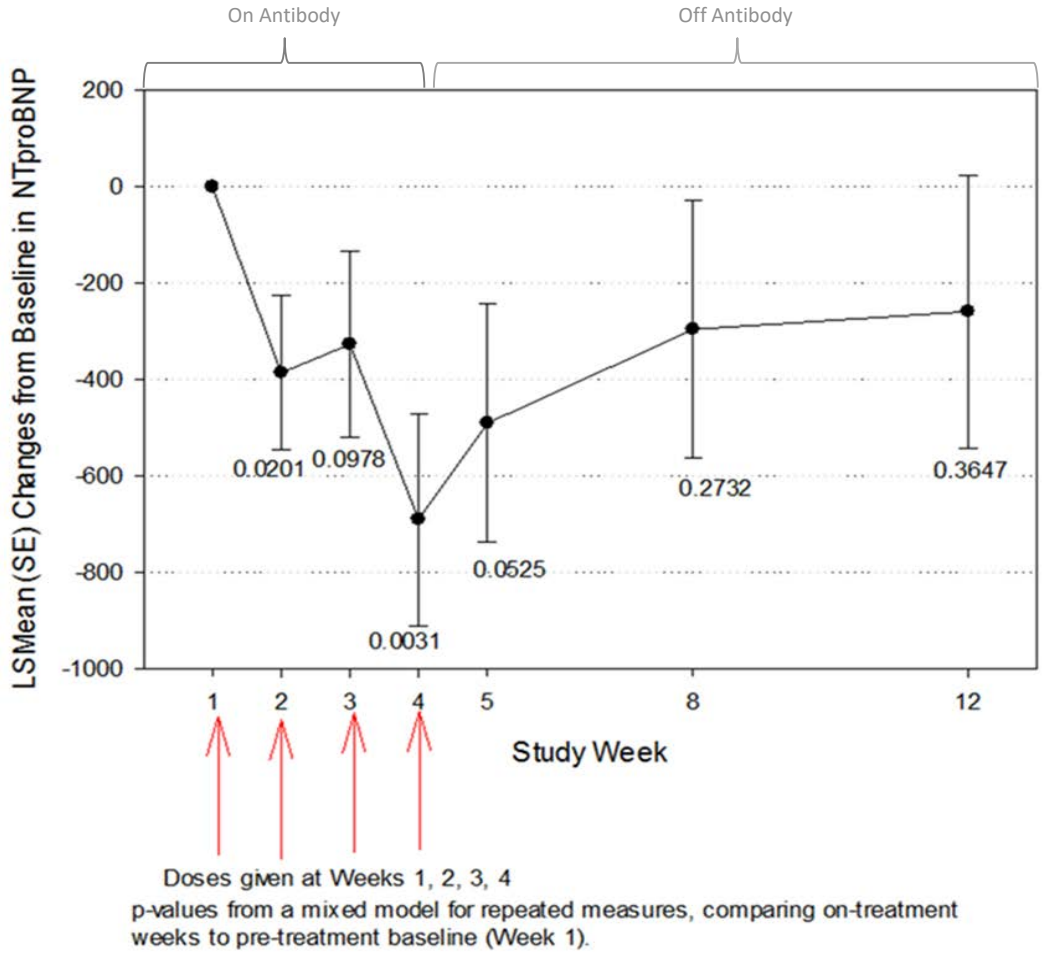
12 patients evaluable for response

Baseline NT-proBNP ≥650 pg/ml and at least one post-baseline NT-proBNP measurement

8 responders – 67%
4 stable

Median time to cardiac response -3 weeks

Sustained Decrease in NT-proBNP After Treatment with CAEL-101 in Phase 1b

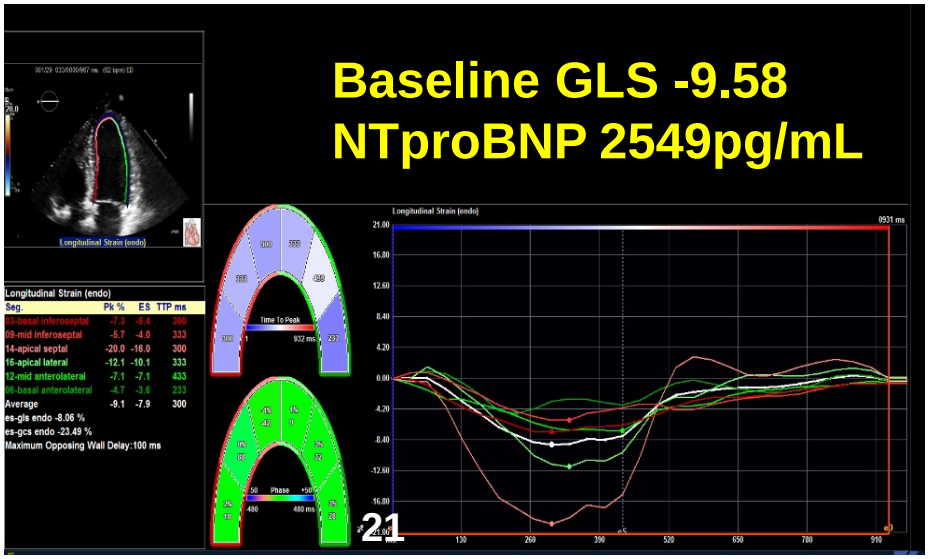


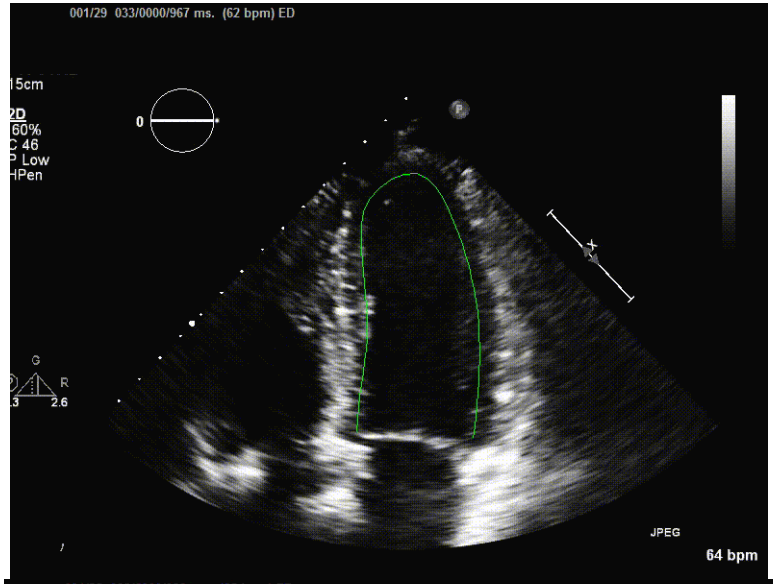
Following 4 weekly doses of CAEL-101, there was a sustained decrease in NT-proBNP from baseline.

CAEL-101 Improves Left Ventricular Global Longitudinal Strain (GLS)

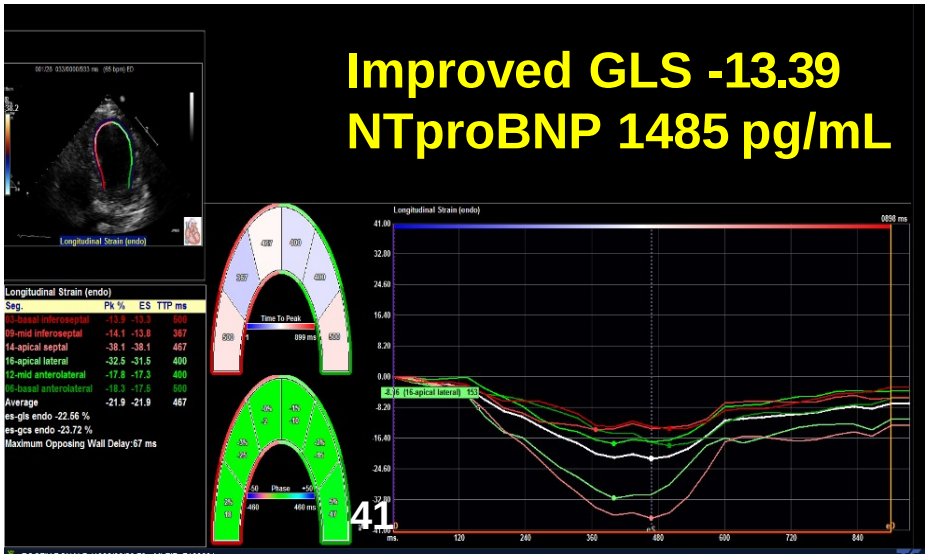
Patient 1-21B, 250mg/m², Dose Level 6

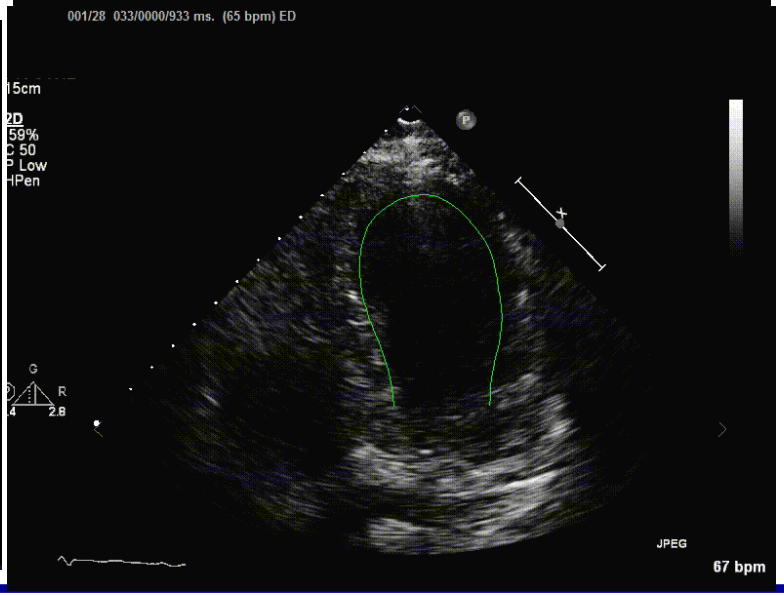
Week 0
Pre-11-1F4 mAb (CAEL-101)





Week 12
Post-11-1F4 mAb (CAEL-101)

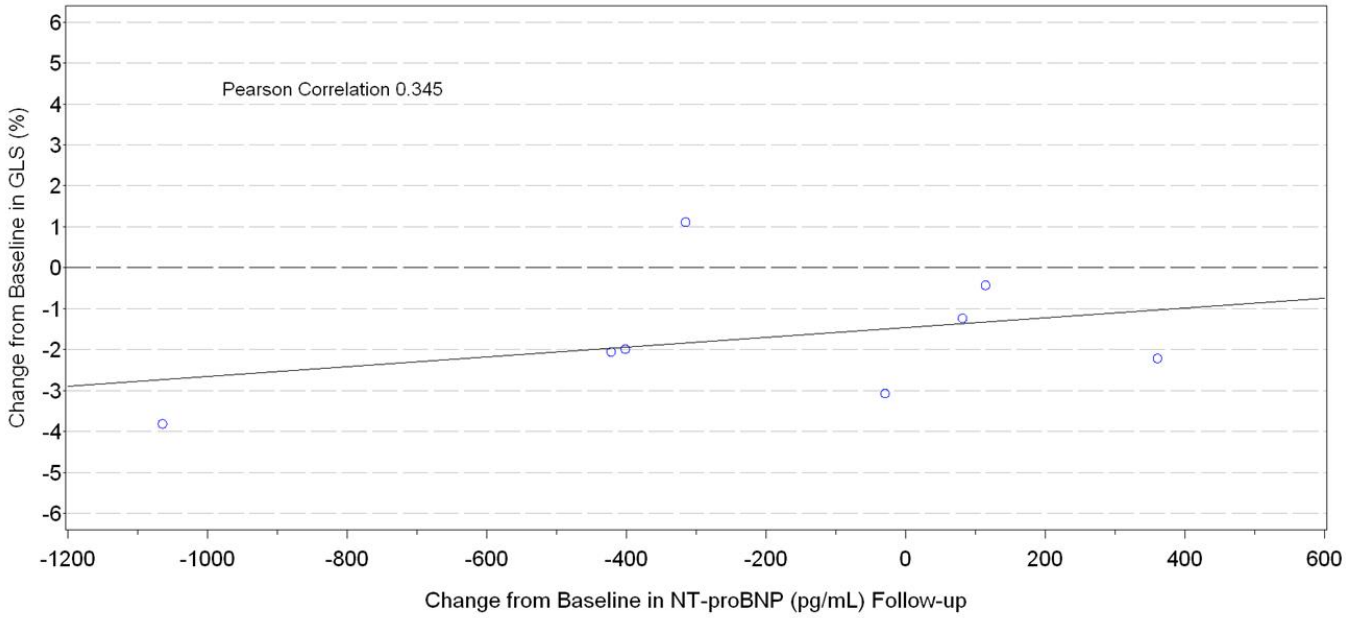




GLS versus Change in NT-proBNP For Cardiac Evaluable Patients Treated with CAEL-101

Caelum Biosciences, Inc.
Protocol: Cael-101

Adhoc Figure 4.0
Scatter Plot of Change from Baseline Global Left Ventricular Strain (GLS) vs. Change NT-proBNP
Population: Cardiac Evaluable Patients - NT-proBNP from Caelum Database



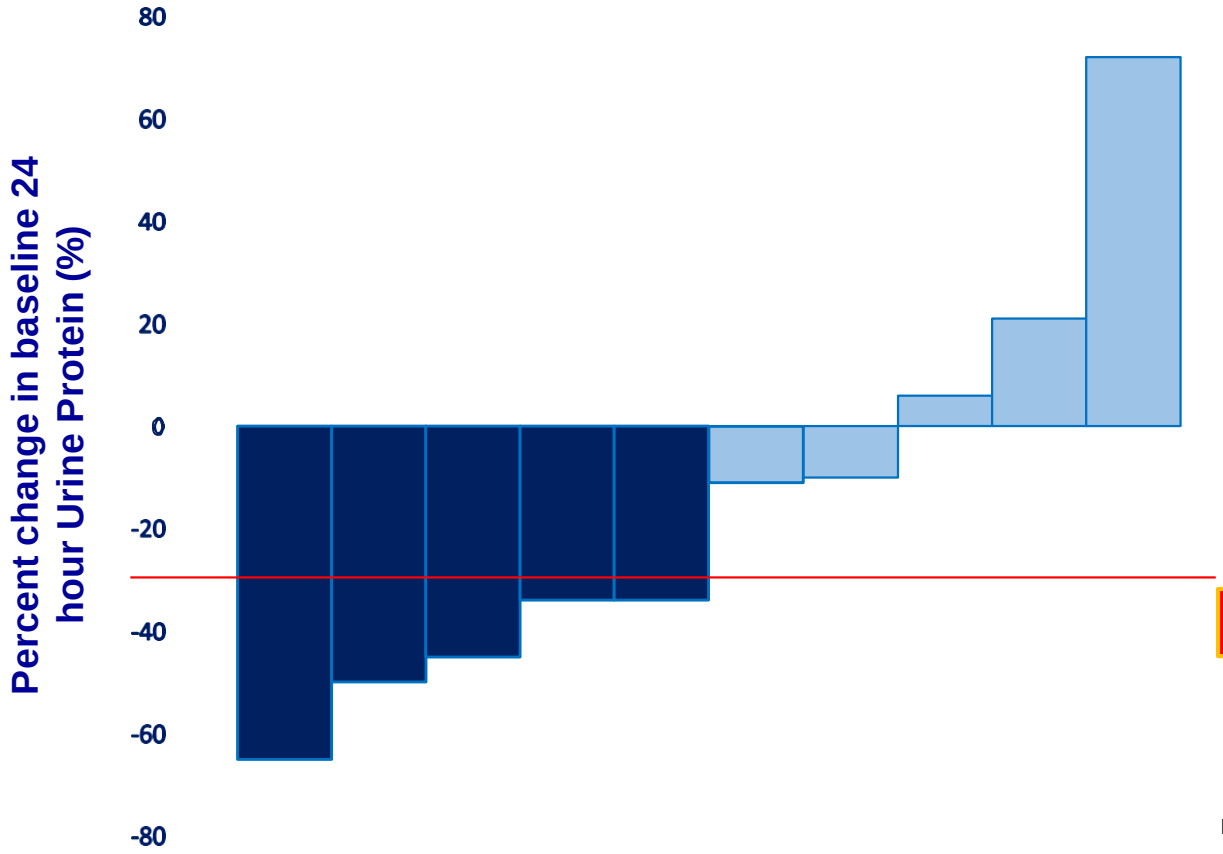
Regression Equation:
gls_chg = -1.458603 + 0.0012*caelum_bnp_chg

Note: Week 1 NT-proBNP was used as Baseline (Caelum)
Source code: C:\Caelum\CAEL-101\outputs\figures\Word\Adhoc_FNTproBNP_GLS.sas Output file: Adhoc_FNTproBNP_GLS.rtf Date/Time Generated: 26JAN2018 3:06

Evaluable patients n = 8

- **An improvement in GLS corresponds to a more negative number.**
- **As NT-proBNP improved, so did GLS.**
- **The Pearson Correlation is 0.345**

Best Renal Response After Treatment with CAEL-101



STABLE

No renal response or progression ≥ 25% decrease in GFR

RESPONSE

≥ 30% decrease in proteinuria from baseline in the absence of renal progression

10 patients evaluable for response

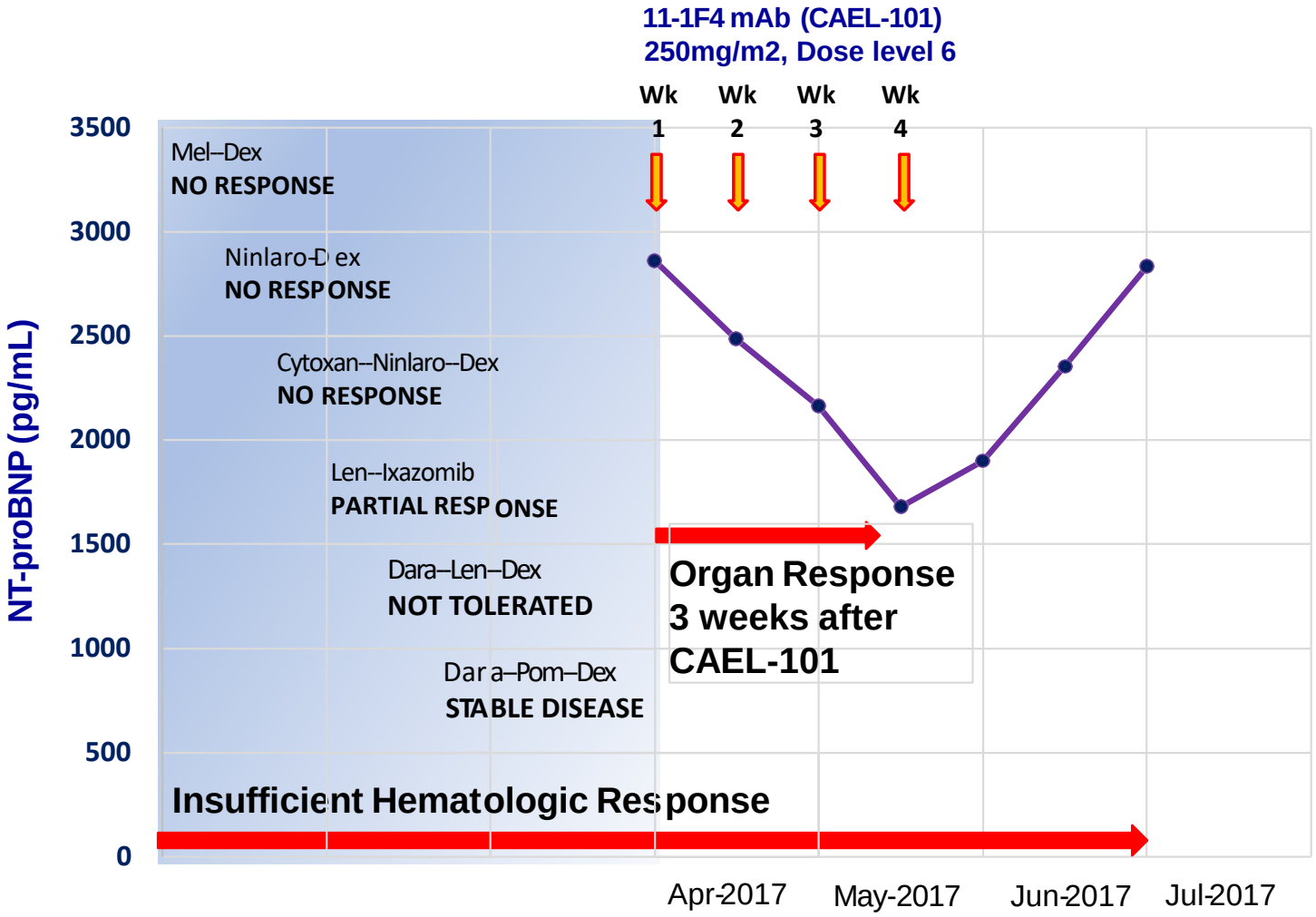
5 responders – 50%

5 stable

Median time to renal response – 4 weeks*

*24 hour urine protein measured at screening and Week 8 in Phase 1a and at screening and Weeks 5, 8 and 12 in Phase 1b

Organ Response Occurs Independent of Depth of Response to Chemotherapy



- Patient with cardiac Lambda AL Amyloidosis
- 6 prior treatments with best Hematologic Response PR
- Prior to CAEL-101 **NO Organ response**

Summary and Future Outlook

- **Treatment with CAEL-101 is well tolerated and safe**

- **CAEL-101 is clinically efficacious**
  - early organ response
  - Cardiac, Renal, GI, Liver and Soft tissue

- **CAEL-101 represents a promising treatment for AL Amyloidosis**
  - reduces amyloid burden and leads to improvement in organ function
  - possible simultaneous induction of hematologic and organ response to:
    - preserve organ function
    - allow for auto-SCT
    - improve survival

- **Multicenter Phase 2 SWOG trial**
- **Phase 3 trial conducted by Caelum Biosciences**

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